These responses are intended to be the basis for a subsequent discussion. Either a revised application or formal response will be submitted later.

§1. I have attached prototypes of Forms 8A and 8B.

§2. In order to show how the figures illustrate the features of the invention, I would like to add the following section to DETAILED DESCRIPTION OF THE INVENTION.

Use of the preferred embodiment: The apparatus must be next to a patient. Place a quartz cuvette into a holder thermostatted at 37°C and allow to equilibrate 15 min. Fix a six-around-one fiber optic probe against the cuvette at an angle of 45°. Couple the central read fiber to a CCD spectrometer, which, in turn, is interfaced to a computer workstation. Couple the six illumination fibers to a 100W tungsten lamp. Shutter the lamp and acquire a spectrum, $D(\lambda)$. Open the shutter. Draw venous blood from the patient into a tube without anticoagulant and immediately transfer into the cuvette. Acquire spectra at the maximum rate of the spectrometer for 20 min. Data will have been stored in the workstation as files containing a series of pairs of numbers, wavelength and light intensity; the name of each file indicates the time of acquisition. Reformat the data as a time course of light intensity at each wavelength. At every wavelength, estimate the counts that would have been reported at t=0, $C^0(\lambda)$, by linear extrapolation from the first 5 recorded values. Reformat the data as relative reflectance, $R(\lambda,t)$. At every wavelength, display the time course of reflected light intensity; the time course will resemble Fig. 1A. There is an initial decrease in relative reflectance that reaches a plateau (Fig. 1A). The time at which the relative reflectance begins to increase from the plateau marks the end of region one (the monotonic decrease) and the beginning of region two (the sigmoidal increase). By the method of least squares, fit the double exponential function (Eq. 1) to the time course of the monotonic decrease; this assigns 5 numeric values to the first region. The sigmoidal increase will end in a plateau, which marks the beginning of the third region (linear region). By the method of least squares, fit the logistic function (Eq. 2) to region two; this assigns 4 numeric values to the second region. The third region ends in an unpredictable manner; however, since it is fit with the equation of a straight line (Eq. 3), the terminus need not be identified precisely. By the method of least squares, fit a straight line to the third region; this assigns 2 numeric values to this portion of the time course. The 11 numeric values assigned at each wavelength characterize the specimen of native blood drawn from this patient.

§§3-9. To address these issues, I would like to add the following text to the beginning of DETAILED DESCRIPTION OF THE INVENTION.

In this application, "blood" refers to whole blood, both native and anticoagulated, and is distinguished from isolated blood components, such as plasma and platelets. The ability to study clotting native blood is one of the unique features of this invention. In this application, "light" refers to that region of the electromagnetic spectrum, 200-900 nm, around what is visible. A particular light source may be characterized by its degree of polarization, coherence, collimation, and range of wavelengths. The ability to collect and use information contained in light signals of various wavelengths (spectral analysis) to study blood clotting is a unique feature of this invention. Light interacts with matter in four ways: reflection, refraction, diffraction, and absorption. Reflection, refraction and diffraction all result in light leaving the specimen; absorption followed by re-emission may also cause light to leave the specimen. Because it is often impossible to identify the mechanism through which light emerges from the specimen, the term "scattering" is used to include all of these processes. When not otherwise characterized, "scattering" often refers to light emerging from the specimen at 90° to the illuminating beam; "forward-scattering" and "back-scattering" are used to

distinguish the measurement of light emerging in the direction of or opposite to the illuminating beam.

If a sphere is imagined around the illuminated specimen, then the beam of light marks one pole where it enters the sphere and another, diametrically opposite, where it would leave the sphere if the specimen had no effect. In this context, "reflection" has a meaning broader than a fundamental interaction of light with a homogeneous phase of matter. It encompasses all light returned by the specimen into the direction of the illuminating beam, i.e., into the hemisphere marked by the light source, and becomes synonymous with "back-scattering." The fraction of light reflected into the hemisphere of the light source is called the albedo. In this context, reflection may be specular (mirror-like, glossy) or diffuse (matte). Diffuse reflection may arise through several fundamental mechanisms: absorption followed by re-emission, multiple refractions, multiple specular reflections, or combinations of these. The measurement of diffusely reflected light offers a unique advantage. The path length of light measured at a phase angle of 90° or 180° is fixed; light at wavelengths absorbed by the specimen may simply not reach the detector. In diffuse reflection, however, path length may vary with wavelength; light that is highly absorbed may nonetheless reach the detector if it is reflected from a superficial layer, because the path length is too short for complete absorption. Light at wavelengths that are absorbed less may be reflected from both superficial and deep layers. Therefore, diffusely reflected light may distinguish events within the specimen at different distances from the illuminated surface. Because activation of the coagulation cascade begins at the surface and proceeds inward, this information may be particularly relevant in the study of blood clotting. The ability to quantify diffuse reflectance at various wavelengths is a unique feature of this invention.

The vast majority of clotting tests are "times," i.e., they are ways to extract information by measuring the time taken for plasma to clot. The simplest of these is the observation of the specimen with a stopwatch and the determination of the time at which the specimen no longer flows. Clots continue to mature and implicitly these measurements divide the biochemical processes into pre-gel and post-gel phases. Optical methods record changes in plasma during pre- and post-gel phases; however, current methods use this information solely to calculate the time of the sol-gel transition. Therefore, even when current methods explicitly recognize different phases in the clotting process, they report the duration of one phase. This invention improves upon previous methods by explicitly focusing on the time course of the various phases of clotting. By fitting the time course of each phase with a mathematical function, parameters are assigned to each phase and give information that could not be obtained from the time of the sol-gel transition.

The specific issue was raised about distinguishing Claim 1 from Claim 4. I envisioned Claim 1 to be as broad as possible and to refer to light sources of any combination of the descriptive terms above. Similarly, Claim 1 would include any kind of detector, including one that did not disperse reflected light into a spectrum. By leaving it unspecified, I intended to include, for example, polarized light. If broadband illumination were used, this detector would report a wavelength-averaged time course. It would not be optimal, but I would like it to be covered by the patent. Claim 4 and all subsequent claims are limited to broadband illumination and spectral analysis of reflected light.

§10. In response to the citations of prior art, I have summarized my findings in the table below. For convenience, I have included the prior art that I cited as well (Riha et al.).

	Claim 1					Claim 4
Citation	Native blood	Diffuse reflection	Partition of time course	Mathematical fit of each partition	Assign parameters	Wavelength dependence
Riha et al.	no	yes	yes	no	no	no
Kim et al.	yes	no	no	no	no	no
Iwasaka et al.	no	no	yes	no	no	no
4,849,340	no	yes	no	no	no	no
6,099,740	no	no	no	no	yes	no
4,252,536	no	yes	yes	no	no	no
4,777,141	no	no	yes	no	no	no
6,084,660	yes	no	yes	no	no	no